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(Review)

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[Intervention Review]

Non-antistreptococcal interventions for acute guttate psoriasis or an acute guttate flare of chronic psoriasis

Annabel Maruani¹, Mahtab Samimi¹, Natasha Stembridge², Rania Abdel Hay³, Elsa Tavernier⁴, Carolyn Hughes⁵, Laurence Le Cleach^{6,7}

¹Department of Dermatology, Université François-Rabelais de Tours, Tours, France. ²Department of Dermatology, Addenbrooke's Hospital, Cambridge, UK. ³Department of Dermatology, Faculty of Medicine, Cairo University, Cairo, Egypt. ⁴Centre d'Investigation Clinique de Tours, INSERM 0202, Université François-Rabelais de Tours, Tours, France. ⁵c/o Cochrane Skin Group, The University of Nottingham, Nottingham, UK. ⁶Department of Dermatology, Hôpital Henri Mondor, Créteil, France. ⁷Epidemiology in dermatology and evaluation of therapeutics (EpiDermE) - EA 7379, Université Paris Est Créteil (UPEC), Créteil, France

Contact address: Annabel Maruani, Department of Dermatology, Université François-Rabelais de Tours, Tours, 37044, France.
annabel.maruani@univ-tours.fr.

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ABSTRACT

Background

Guttate psoriasis displays distinctive epidemiological and clinical features, making it a separate entity within the heterogeneous group of cutaneous psoriasis types. It is associated with genetic, immune, and environmental factors (such as stress and infections) and usually arises in younger age groups (including children, teenagers, and young adults). There is currently no cure for psoriasis, but various treatments can help to relieve the symptoms and signs. The objectives of treatment when managing an acute flare of guttate psoriasis are to reduce time to clearance and induction of long-term remission after resolution. This is an update of a Cochrane Review first published in 2000; since then, new treatments have expanded the therapeutic spectrum of systemic treatments used for psoriasis.

Objectives

To assess the effects of non-antistreptococcal interventions for acute guttate psoriasis or an acute guttate flare of chronic psoriasis.

Search methods

We searched the following databases up to June 2018: the Cochrane Skin Specialised Register, CENTRAL, MEDLINE, Embase, and LILACS. We searched five trials registers and checked the reference lists of included studies for further references to relevant randomised controlled trials. We checked the proceedings of key dermatology conferences from 2004 to 2018, and also searched for trials in the US Food and Drug Administration (FDA) database for drug registration.

Selection criteria

All randomised controlled trials assessing the effects of treatments for acute guttate psoriasis or an acute guttate flare of chronic psoriasis clinically diagnosed in children and adults. This included all topical and systemic drugs, biological therapy, phototherapy (all forms: topical and systemic), and complementary and alternative therapies. We compared these treatments against placebo or against another treatment. We did not include studies on drugs that aim to eradicate streptococcal infection. We did not include studies when separate results for guttate psoriasis participants were not available.

Data collection and analysis

Two review authors independently assessed study eligibility and methodological quality and extracted data. We used standard methodological procedures expected by Cochrane. Our primary outcomes were 'percentage of participants clear or almost clear (i.e. obtaining Psoriasis Area Severity Index (PASI) 100/90 and/or Physician's Global Assessment (PGA) of 0 or 1)' and 'percentage of participants with adverse effects and severe adverse effects'. Our secondary outcomes were 'number of relapses of guttate psoriasis or flares within a period of six months after the treatment has finished', 'percentage of participants achieving a PASI 75 or PGA of 1 or 2', and 'improvement in participant satisfaction measures and quality of life assessment measures'. We used GRADE to assess the quality of the evidence for each outcome.

Main results

This review included only one trial (21 participants), which compared fish oil-derived (n-3) fatty acid-based lipid emulsion (50 mL per infusion (1.05 g eicosapentaenoic and 10.5 g docosahexaenoic acid)) (10 participants) to soya oil-derived (n-6) fatty acid-based lipid emulsion (50 mL per infusion (1.05 g eicosapentaenoic and 10.5 g docosahexaenoic acid)) (11 participants) administered intravenously twice daily for 10 days, with a total follow-up of 40 days. The study was conducted in a single centre in Germany in 18 men and three women, aged between 21 and 65 years, who were in hospital with acute guttate psoriasis and had mean total body surface involvement of $25.7\% \pm 20.4\%$ (range 10 to 90). The study was funded by a company that produces the oil emulsions. We found no other evidence regarding non-antistreptococcal interventions used in clinical practice for guttate psoriasis, such as topical treatments (corticosteroids, vitamin D₃ analogues), systemic drugs, biological therapy, and phototherapy.

The primary outcomes of the review were not measured, and only one of our secondary outcomes was measured: improvement in participant satisfaction measures and quality of life assessment measures. However, the study authors did report that there was rare skin irritation at the site of peripheral intravenous route, but the number of affected participants was not provided.

Improvement between baseline and day 10, using a non-validated score assessed by participants themselves daily based on five items (appearance of lesions, impairment of daily life, pruritus, burning, and pain), was greater in the group that received the fish oil-derived (n-3) fatty acid-based lipid emulsion (75%) than in the group receiving the soya oil-derived (n-6) fatty acid-based lipid emulsion (18%) (one trial, 21 participants). However, these results are uncertain as they are based on very low-quality evidence.

Authors' conclusions

There is no evidence regarding topical and systemic drugs, biotherapy, or phototherapy in guttate psoriasis (we did not consider drugs that aimed to eradicate streptococcal infection because these are assessed in another Cochrane Review). We are uncertain of the effect of intravenously administered lipid emulsion on guttate psoriasis because the quality of the evidence is very low, due to risk of bias (unclear risk of bias for all domains), indirectness (the trial only included adults, and the follow-up from baseline was only 10 days), and imprecision (small number of participants).

This review highlights the need for trials assessing the efficacy and safety of phototherapy and topical and systemic drugs for guttate psoriasis. There is also a need for studies that clearly distinguish the specific population with guttate psoriasis from the larger group of people with chronic plaque psoriasis, and children and young adults should be assessed as a distinct group.

PLAIN LANGUAGE SUMMARY

Treatments for acute guttate psoriasis, excluding drugs aimed at treating infection caused by *Streptococcus* bacteria

Review question

The aim of this review was to find out how well different non-antistreptococcal treatments (i.e. drugs not aimed at eradicating streptococcal infection) work for treating acute guttate psoriasis or an acute guttate flare of chronic psoriasis in adults and children, and how safe they are when compared against placebo (an identical but inactive treatment) or another treatment. This was important because there is a lack of information and evidence about the best way to treat guttate psoriasis. We collected and analysed all relevant studies to answer this question and found one study.

Background

Psoriasis is a chronic skin disease characterised by patches of red, flaky skin covered with scales (known as plaques). Approximately 2% of people have psoriasis. Guttate psoriasis is a type of psoriasis that is characterised by smaller lesions and is more common in children and young people. Treatments for guttate psoriasis aim to clear the skin of lesions for as long as possible, and include topical (applied to the skin) or oral (taken by mouth) medicines; phototherapy (i.e. ultraviolet light therapy); and biological medicines (whereby a living organism creates the active substance). It is not known which of these treatments work best at clearing lesions in guttate psoriasis and whether they are safe.

Study characteristics

We found one relevant study that compared the effects of giving injections into the vein of two different lipid (fat) emulsions twice daily for 10 days: one emulsion (two or more liquids that are often unmixable) was derived from fish oil, and the other was derived from soya oil. Participants were followed for a total of 40 days. The study was conducted in Germany in 21 adults (18 men and 3 women) aged 21 to 65 years, with a mean of involved skin surface of 25%, who were in hospital with acute guttate psoriasis. The study was funded by the company that produces the oil emulsions.

Key results

Treatments for which we found no evidence include phototherapy and topical, oral, and biological medicines. The only study identified did not measure our two primary outcomes: percentage of people treated whose skin became clear (or almost clear) of lesions; and the side effects, or harms, of the treatments.

Most of our secondary outcomes were also not measured, including worsening of guttate psoriasis or recurrence within a period of six months after the treatment has finished; and percentage of participants achieving a Psoriasis Area Severity Index 75 or Physician's Global Assessment of 1 or 2. The included study did not report measuring any harms of the treatments; however, the study authors did report rare skin irritation at site of injection, but did not provide the number of affected participants.

The study participants rated some outcomes themselves, including the appearance of the skin lesions, the effects on their daily life, itching, burning, and pain. After 10 days of treatment, study participants who received the fish oil-derived lipid emulsion (75% of people in this group) rated greater improvements than those receiving the soya oil-derived lipid emulsion (18% of people in this group). However, these results are uncertain as they are based on very low-quality evidence.

The evidence is current to June 2018.

Quality of the evidence

We rated the quality of the available evidence as very low.

We considered that the study may be at risk of bias due to limitations in its design, and only a small number of people were included in the study. In addition, the study only enrolled adults, although guttate psoriasis is more common in children.

SUMMARY OF FINDINGS

Summary of findings for the main comparison. Intravenous soya oil-derived (n-6) fatty acid-based lipid emulsion compared to intravenous fish oil-derived (n-3) fatty acid-based lipid emulsion for guttate psoriasis

Intravenous soya oil-derived (n-6) fatty acid-based lipid emulsion compared to intravenous fish oil-derived (n-3) fatty acid-based lipid emulsion for guttate psoriasis

Patient or population: guttate psoriasis

Setting: hospital

Intervention: intravenous soya oil-derived (n-6) fatty acid-based lipid emulsion

Comparison: intravenous fish oil-derived (n-3) fatty acid-based lipid emulsion

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	Nº of participants (studies)	Quality of the evidence (GRADE)	Comments
	Risk with intravenous fish oil-derived (n-3) fatty acid-based lipid emulsion	Risk with intravenous soya oil-derived (n-6) fatty acid-based lipid emulsion				
Percentage of participants clear or almost clear, i.e. obtaining PASI 100/90 and/or PGA of 0 or 1 in the short term	-	-	-	-	-	Not measured
Percentage of participants with adverse effects and severe adverse effects	-	-	-	-	-	Not measured. However, the study authors reported that there was rare skin irritation at the site of peripheral intravenous route, but did not provide the number of affected participants.
Number of relapses of guttate psoriasis or flares within a period of 6 months after the treatment has finished	-	-	-	-	-	Not measured
Percentage of participants achieving a PASI 75 or PGA of 1 or 2	-	-	-	-	-	Not measured

Improvement in participant satisfaction measures and quality of life assessment measures	See comment	See comment	-	21 (1 RCT)	⊕⊕⊕⊕ VERY LOW ¹	<p>The score improved from 19.1 on day zero to 33.4 on day 10 (change = 14.3 points, or 75% improvement between baseline and 10 days) in intravenous fish oil-derived (n-3) fatty acid-based lipid emulsion group.</p> <p>The score improved from 25.4 on day zero to 30 on day 10 (change = 4.6 points, or 18% improvement between baseline and 10 days) in soya oil-derived (n-6) fatty acid-based lipid emulsion group.</p> <p>The associated standard deviations (or confidence intervals) were not provided.</p>
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***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **PASI:** Psoriasis Area Severity Index; **PGA:** Physician's Global Assessment; **RCT:** randomised controlled trial

GRADE Working Group grades of evidence

High quality: We are very confident that the true effect lies close to that of the estimate of the effect.

Moderate quality: We are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Low quality: Our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.

Very low quality: We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

¹Downgraded by three levels to very low quality: one level due to risk of bias (was assessed as unclear for all items, except risk of attrition bias considered as low); one level due to indirectness (only adults with a mean age of 37 years for a disease occurring in children and young adults; hospitalisation for a disease that does not require hospitalisation; no long-term follow-up); and imprecision (one small trial).

BACKGROUND

Description of the condition

The term 'guttate psoriasis' refers to a subtype of cutaneous psoriasis defined by its clinical presentation, that is the sudden onset of small (generally less than 1 cm in size), monomorphic, erythematous and squamous macules or papules, appearing as

droplets ('gutta'), mainly spread over the trunk and limbs (Figure 1; Figure 2). At disease onset, guttate psoriasis may occur on its own (as acute guttate psoriasis) or during the clinical course of a chronic plaque psoriasis flare (a guttate flare of chronic plaque psoriasis). The guttate phenotype has been reported to represent 18% to 30% of clinical phenotypes, and Mallbris and colleagues observed it at the onset of psoriasis in a study of 400 adults (Kwon 2012; Mallbris 2005).

Figure 1. Guttate psoriasis.



Figure 2. Guttate psoriasis.

Guttate psoriasis displays distinctive epidemiological and clinical features, making it a separate entity within the heterogeneous group of cutaneous psoriasis types. As with other subtypes of psoriasis, the diagnosis of guttate psoriasis is usually clinical, based on examination of the skin. Sometimes, histological examination of a skin biopsy may be necessary for differential diagnosis, and this typically shows hyperkeratosis, parakeratosis (incomplete development of keratinocytes), dilated capillaries in the dermis, and neutrophils in the stratum corneum.

The pathogenesis of guttate psoriasis is complex and multifactorial, as is the case with other types of psoriasis. Guttate psoriasis is associated with genetic, immunological, and environmental factors (such as stress and infections) and usually arises in the young (including children, teenagers, and young adults). A family history of psoriasis appears to be a risk factor and was found in frequencies ranging from 11.1% to 48.9% of people with this condition (Ko 2010; Mallbris 2005; Naldi 2001). In chronic plaque psoriasis, the guttate subtype has been suggested to be associated with the *PSORS1* gene susceptibility alleles (Asumalahti 2003). Dysregulation of immune cells in the skin plays a central role in the pathogenesis of psoriasis, involving Th1 and Th17 cells, innate immune cells, and regulatory T cells (Cai 2012). Differential expression and regulatory functioning for inflammatory cytokine production by T cells has been found in plaque and guttate psoriasis and may account for their differences in pathogenesis (Yan 2010).

Infectious events have a substantial triggering role in guttate psoriasis, since the eruption typically occurs one to three weeks after a history of a streptococcal upper respiratory tract infection (Naldi 2001; Telfer 1992). Overall, a triggering streptococcal pharyngitis was found to be nine times more common in people with guttate than non-guttate psoriasis (Mallbris 2005). The streptococcal infection may activate the alternative complement pathway and trigger cross-reactivity between streptococcal antigens and the human epidermis (Leung 1993; Perez-Lorenzo 1998; Zhao 2005). Cases of guttate psoriasis triggered after the use of biologics, especially tumour necrosis factor (TNF) antagonists, have also been reported (Collamer 2010).

Few studies have investigated the long-term course after the initial onset of guttate psoriasis. The acute flare usually spontaneously resolves within a few weeks or months; however, a person may experience successive flares of guttate psoriasis after variable symptom-free intervals. Approximately 30% to 68% of people with an acute flare progress to chronic psoriasis, but this is based on sparse data from only three studies involving 15, 62, and 26 participants, respectively, with acute guttate psoriasis (Ko 2010; Martin 1996; Williams 1976). It has been suggested that young people with a triggering upper respiratory tract infection are more likely to experience a long-term remission of the disease after the first acute flare (Ko 2010).

Several instruments have been developed for assessment of the clinical severity of cutaneous psoriasis, the most commonly used being the Psoriasis Area Severity Index (PASI) score. The PASI score is based on the evaluation of the proportion of body surface affected and the degree of plaque redness, thickness, and scaling, but it is difficult to use for assessment of the guttate subtype because of the dissemination of the lesions over the body. Other usual instruments are the Physician's Global Assessment (PGA), and achievement of optimal quality of life, assessed by the Dermatology Life Quality Index (DLQI). No separate instrument has been developed for this specific subtype of psoriasis ([Mrowietz 2011](#); [Spuls 2010](#)).

Description of the intervention

There is currently no cure for psoriasis, but various treatments can help to relieve the symptoms. The objectives of treatment when managing an acute flare of guttate psoriasis are to achieve skin clearance and induction of long-term remission after resolution. Long-term maintenance treatment may be necessary for those who experience chronic guttate psoriasis.

The available treatments for cutaneous psoriasis have been evaluated mostly in people with the plaque psoriasis subtype, with no clear evidence for their efficacy in guttate psoriasis. The current therapeutic regimens for cutaneous psoriasis include topical and systemic treatments.

First-line therapy includes topical treatments (corticosteroids, vitamin D₃ and its analogues, retinoids, tar) ([Dubertret 1992](#); [Highton 1995](#); [Samarasekera 2013](#); [Weinstein 1997](#); [Weinstein 2003](#)). For guttate psoriasis, antistreptococcal interventions (oral antibiotics or tonsillectomy) are also prescribed; however, they are out the scope of this review as they are already covered in another review ([Dupire 2019](#); [Hone 1996](#); [Rachakonda 2015](#)).

Second-line therapy consists of phototherapy and systemic non-biological drugs, that is retinoids, ciclosporin, and methotrexate ([Christophers 1992](#); [Koo 1998](#); [Pettit 1979](#); [Saurat 2008](#)). Phototherapy includes broad-band ultraviolet B (UVB) (254 to 313 nm), narrow-band UVB (311 to 313 nm), and psoralen ultraviolet A (PUVA) ([Menter 2010](#)). It is often relevant for the treatment of guttate psoriasis because of the dissemination of psoriatic lesions over the body, except in young children.

Third-line therapy refers to biological treatments, which have recently expanded the therapeutic spectrum of systemic treatments for psoriasis. They include tumour necrosis factor- α (TNF- α) antagonists (infliximab, etanercept, adalimumab) and the monoclonal antibody ustekinumab, which targets interleukin-12 and -23 (IL-12/23). The following molecules have all had at least one evaluation of their effectiveness against placebo: alefacept ([Krueger 2002](#); [Lebwohl 2003](#)), etanercept ([Leonardi 2003](#)), infliximab ([Chaudhari 2001](#)), adalimumab ([Menter 2008](#)), ustekinumab ([Lebwohl 2010](#)).

How the intervention might work

Corticosteroids exhibit anti-inflammatory, antiproliferative, immunosuppressive, and vasoconstrictive effects. They can regulate transcription of gene coding for proinflammatory cytokines, after binding to intracellular corticosteroid receptors. Their use in children is possible.

Retinoids are derivatives of vitamin A, which is involved in the growth and differentiation of skin tissue. Retinoids bind to the nuclear receptors that belong to the large family of steroid hormone receptors. Proteins modulated by retinoids are manifold: epidermal structural proteins, metalloproteinases, cytokines ([Goldfarb 1988](#)). Retinoids promote normalisation of abnormal keratinocyte differentiation by a decrease in keratinocyte hyperproliferation and the expression of inflammatory markers. Topical and systemic retinoids are used in psoriasis. There are no available data for their use in children.

Phototherapy exhibits immunosuppressive effects; inhibits keratinocyte hyperproliferation and angiogenesis (formation of new blood vessels); and decreases T lymphocytes in psoriasis lesions by apoptosis (programmed cell death).

Ciclosporin is an oral immunosuppressive agent that inhibits the initial phase of the activation of CD4 T cells, leading to the absence of synthesis of interleukin-2 (IL-2) (blocking transcription of IL-2 by the complex cyclophilin-ciclosporin) ([Ho 1996](#); [Ho 2001](#)). This immunosuppression is rapid and reversible.

Methotrexate is an antimetabolite that acts as an antagonist of folic acid. Low doses of methotrexate exert anti-inflammatory and immunomodulatory activities.

Among biological therapies, two monoclonal antibodies against TNF- α (infliximab, adalimumab) and one recombinant TNF- α receptor (etanercept) have been developed to inhibit TNF- α signalling, thus preventing its inflammatory effects.

Why it is important to do this review

Reliable data to inform the management of guttate psoriasis appear to be limited. It is not known whether the therapeutic strategies for guttate psoriasis should differ according to population (children, teenagers, adults), clinical history (family history of psoriasis, infectious triggering event), clinical evolution (duration of the eruption, recurring flares, chronic course), or treatment goals (clearance of the acute flare, prevention of subsequent flares, or evolution into a chronic course).

The previous Cochrane Review on this subject, which included data up until 1999 ([Chalmers 2000](#); [Chalmers 2001](#)), did not identify any trials of commonly used topical therapies or phototherapy, and found very little evidence to guide healthcare professionals and their patients in the management of guttate psoriasis. Since this systematic review, biological treatments have expanded the therapeutic spectrum of systemic treatments used for psoriasis (infliximab, etanercept, adalimumab, ustekinumab). In one Cochrane Review assessing the effects of narrow-band (NB) UVB phototherapy versus broad-band UVB or PUVA photochemotherapy for psoriasis ([Chen 2013](#)), the authors concluded that NB-UVB plus retinoid and PUVA plus retinoid are similarly effective in treating people with chronic plaque psoriasis or guttate psoriasis.

The plans for this update of the Cochrane Review, first published in 2000 ([Chalmers 2000](#)), were published with a new protocol 'Interventions for guttate psoriasis' ([Maruani 2015](#)).

A separate systematic review addressed antistreptococcal therapeutic strategies for guttate and chronic plaque psoriasis

(Owen 2000). An update of that review has been published (Dupire 2019).

OBJECTIVES

To assess the effects of non-antistreptococcal interventions for acute guttate psoriasis or an acute guttate flare of chronic psoriasis.

METHODS

Criteria for considering studies for this review

Types of studies

All randomised controlled trials (RCTs) were eligible for inclusion. Cross-over trials were eligible, but because of the unpredictable evolution of guttate psoriasis and the risk of carry-over bias, we planned to analyse only the first period in such studies.

Types of participants

We included studies of children and adults with acute guttate psoriasis or an acute guttate flare of chronic psoriasis. The diagnosis of guttate psoriasis was clinical and based on skin examination. Participants could be at any line of treatment. We excluded trials that did not have separate data for guttate psoriasis patients (not available in published or unpublished data or through requests to the author).

Types of interventions

We included any intervention, including all topical and systemic drugs, biological therapy, phototherapy (all forms: topical and systemic), and complementary and alternative therapies, whatever their status of licensing. We included studies assessing combined therapies, as well as cases where antistreptococcal therapy was used as concomitant therapy. We compared one treatment against placebo or against another treatment.

We did not include drugs that aimed to eradicate streptococcal infection, which are assessed in another Cochrane Review (Dupire 2019).

Types of outcome measures

Psoriasis is a chronic disease in which treatments are often given when symptoms are acute, with a return to baseline after discontinuation of the treatment. The primary endpoint should be clinically relevant to the person with the disease (www.comet-initiative.org). The Psoriasis Area Severity Index (PASI) 75, that is 75% improvement in the PASI, is the primary endpoint used in most clinical trials that evaluate psoriasis treatments, but is difficult to use for assessment of the guttate subtype, where there are numerous plaques of small size. The Physician's Global Assessment (PGA) score of 0 is 'clear' and > 1 means increasing severity. Participants becoming clear or almost clear in the short term and absence of relapses in the long term are more stringent and reliable criteria by which to measure improvement.

Primary outcomes

1. Percentage of participants clear or almost clear, i.e. obtaining PASI 100/90 and/or PGA of 0 or 1 in the short term (up to 8 weeks of treatment).
2. Percentage of participants with adverse effects and severe adverse effects.

Secondary outcomes

1. Number of relapses of guttate psoriasis or flares within a period of six months after the treatment has finished.
2. Percentage of participants achieving a PASI 75 or PGA of 1 or 2. It is unlikely that PASI 75 would have been reported in older trials, so we planned to calculate this based on the percentage reduction in PASI (when this information was available).
3. Improvement in participant satisfaction measures and quality of life assessment measures.

Search methods for identification of studies

We aimed to identify all relevant RCTs regardless of language or publication status (published, unpublished, in press, or in progress).

Electronic searches

The Cochrane Skin Information Specialist searched the following databases up to 7 June 2018 using strategies based on the draft strategy for MEDLINE in our published protocol (Maruani 2015):

1. the Cochrane Skin Specialised Register using the search strategy in [Appendix 1](#);
2. the Cochrane Central Register of Controlled Trials (CENTRAL) 2018, Issue 5, in the Cochrane Library using the strategy in [Appendix 2](#);
3. MEDLINE via Ovid (from 1946) using the strategy in [Appendix 3](#);
4. Embase via Ovid (from 1974) using the strategy in [Appendix 4](#); and
5. LILACS (Latin American and Caribbean Health Science Information database, from 1982) using the strategy in [Appendix 5](#).

Trials registers

Two review authors (AM, MS) searched the following trials registers up to 7 June 2018 using the keywords 'guttate psoriasis':

1. ISRCTN registry (www.isrctn.com);
2. US National Institutes of Health Ongoing Trials Register ClinicalTrials.gov (www.clinicaltrials.gov);
3. Australian New Zealand Clinical Trials Registry (www.anzctr.org.au);
4. World Health Organization International Clinical Trials Registry Platform (WHO ICTRP) (apps.who.int/trialsearch/); and
5. EU Clinical Trials Register (www.clinicaltrialsregister.eu).

We also searched for trials in the US Food and Drug Administration (FDA) database for drug registration (www.accessdata.fda.gov/scripts/cder/drugsatfda/).

Searching other resources

References from included studies

We checked the bibliographies of included studies for further references to relevant trials.

Conferences

We checked the proceedings of the following conferences from 2004 to 2018, except the years that Cochrane Skin previously searched for the CENTRAL database:

- American Academy of Dermatology (AAD) (except 2006, 2007, 2010, and 2011);
- Society for Investigative Dermatology (SID) (except 2004, 2005, 2006, 2010, and 2011); and
- European Academy of Dermatology and Venereology (EADV) (except 2005 and 2006).

Adverse effects

We did not perform a separate search for adverse events of interventions used for the treatment of guttate psoriasis. We examined data on adverse events from the studies included in the review.

Data collection and analysis

We used GRADEpro GDT to create a 'Summary of findings' table in the review in which we summarised the primary outcomes for the most important comparison, using GRADE to interpret the results (see Section 12.2 of the *Cochrane Handbook for Systematic Reviews of Interventions*) (GRADEpro GDT; Schünemann 2011).

Selection of studies

Two review authors (AM, NS) independently examined each title and abstract to exclude irrelevant reports, and independently examined full-text articles to determine eligibility. We contacted study authors for clarification when necessary. The review authors discussed disagreements to reach consensus. We listed excluded studies and documented the primary reason for exclusion.

Data extraction and management

Two review authors (MS, RAH) independently extracted the data from published and unpublished reports using a standardised data extraction form that the team had piloted on a set of included trials. A third review author (LLC) resolved any disagreements on data extraction between the two review authors. To populate the [Characteristics of included studies](#) table, we extracted the following data from each included trial: study design, inclusion and exclusion criteria, baseline characteristics of the total number of participants randomised to each intervention, description of interventions, and description of outcomes. One review author (AM) checked and entered the data into Review Manager 5 software (RevMan 2014).

Assessment of risk of bias in included studies

Two review authors (MS, RAH) separately used the Cochrane's 'Risk of bias' tool to assess risk of bias in the included studies, grading it as 'low', 'high', or 'unclear' for each of the following domains and according to the following general principles (see Section 8.4 of the *Cochrane Handbook for Systematic Reviews of Interventions*) (Higgins 2011a). In case of disagreement the methodologist (ET) was consulted to reach consensus.

1) Selection bias

- Was the allocation sequence adequately generated? We considered randomisation as adequate if the allocation sequence was generated from a table of random numbers or by computer. We considered it inadequate if sequences could be related to prognosis. We considered it unclear if it was stated that the trial was randomised, but the method of randomisation was not described.

- Was allocation adequately concealed? We deemed allocation concealment as adequate if the report states that it was undertaken by means of sequentially pre-numbered, sealed, opaque envelopes, or by a centralised system.

2) Performance and detection bias

- Was blinding feasible? Was knowledge of the allocated intervention adequately prevented during the study? We evaluated the risk of bias associated with inadequate blinding separately for personnel and participants, outcome assessors, and each outcome.

3) Attrition bias

- Were incomplete outcome data adequately addressed? We examined if there was imbalance across intervention groups in numbers or reasons for missing data, type of measures undertaken to handle missing data, and whether the analysis was carried out as intention-to-treat. We assessed the use of strategies to handle missing data (last observation carried forward, multiple imputation, etc.).

4) Reporting bias

- Are reports of the study free of the suggestion of selective outcome reporting? We evaluated if each outcome was measured, analysed, and reported. We compared outcomes specified in the protocols of the included studies (if available on the FDA website or ClinicalTrials.gov) and in material and methods to outcomes presented in the results section.

We did not assess the domain 'other bias', as we did not identify any specific methodological concerns that were not already covered in the other 'Risk of bias' domains.

Measures of treatment effect

For dichotomous outcomes, we planned to calculate risk ratios (RR) with 95% confidence intervals (CI). For continuous outcomes, we planned to calculate mean differences (MD) with 95% confidence intervals. For continuous outcomes with different measurement scales in different RCTs, we planned to calculate standardised mean differences (SMD) with 95% CI (see Chapter 9 of the *Cochrane Handbook for Systematic Reviews of Interventions*) (Deeks 2011).

Unit of analysis issues

The primary unit of analysis was the participant. In case of cross-over trials, we planned to analyse data from the first period. In case of multi-arm trials, we compared arms two at a time in separate comparisons. In case of multidose trials, we planned to group together all the different dose groups to compare them collectively with the control group.

Dealing with missing data

In the case of missing data, we attempted to email trial authors for further information (Table 1). If missing outcome data were not available from the study report or from the authors, we planned to use simple imputation methods, and assume that all missing data were either events or non-events (Chapter 16: Special topics in statistics, Higgins 2011b). The data reported in the only included study did not permit use of this method.

Assessment of heterogeneity

We planned to assess statistical heterogeneity by visual inspection of the forest plots and by calculating the Q and I^2 statistics, and to interpret the I^2 statistic value according to the following thresholds (see Section 9.5.2 of the *Cochrane Handbook for Systematic Reviews of Interventions*) (Deeks 2011): 0% to 40% might not be important; 30% to 60% may represent moderate heterogeneity; 50% to 90% may represent substantial heterogeneity; 75% to 100% represents considerable heterogeneity.

Potential sources of heterogeneity or inconsistency included participant baseline characteristics (age, weight, duration of psoriasis), treatment doses, and duration of treatment. We planned to investigate the distributions of these characteristics across groups and studies.

Assessment of reporting biases

To address publication bias, we planned to draw contour-enhanced funnel plots for each meta-analysis if 10 or more studies contributed data (Egger 1997).

Data synthesis

We planned to conduct data synthesis using the Review Manager 5 software provided by Cochrane (RevMan 2014). We would perform data analysis according to the recommendations in Chapter 9 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Deeks 2011). For all analyses, we planned to employ random-effects models, providing that at least three studies were available, and synthesise data as analysed in each trial.

Subgroup analysis and investigation of heterogeneity

We planned to investigate the influence of age (children versus adults), and distinguished de novo guttate psoriasis from acute guttate flares of chronic psoriasis. In cases where antistreptococcal

therapy was used as concomitant therapy, we planned to perform subgroup analyses as follows: no antistreptococcal concomitant therapy; current antistreptococcal concomitant therapy.

Sensitivity analysis

Providing there were sufficient trials in the meta-analyses, we planned to perform a sensitivity analysis showing how conclusions might be affected if only studies at low risk of bias were included. We also planned to perform sensitivity analysis using fixed-effect models and report these if a difference in interpretation existed after comparison with the random-effects model. We planned to perform sensitivity analysis to assess how sensitive results were to reasonable changes in the assumptions that we might have made.

RESULTS

Description of studies

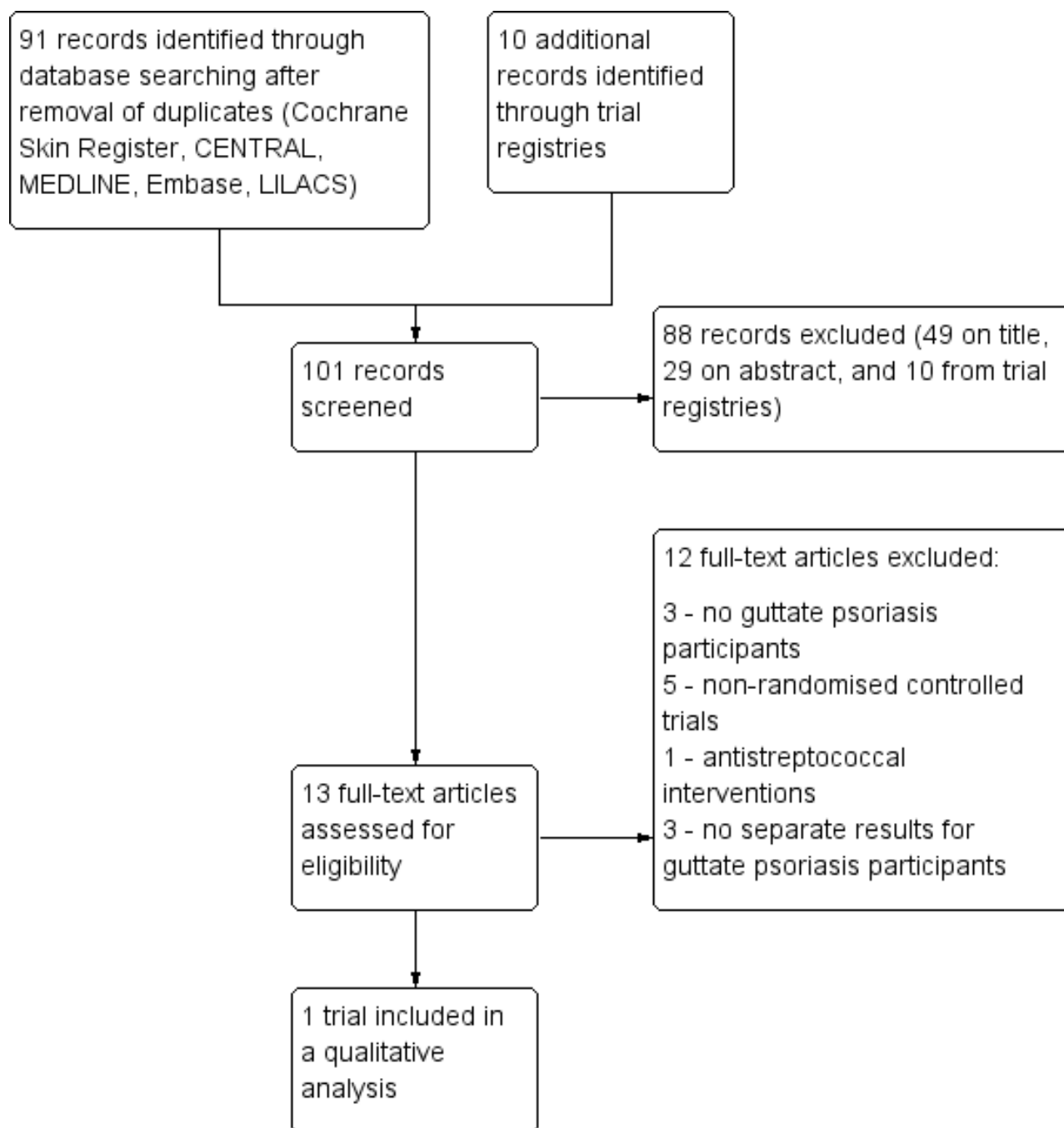
Details on the characteristics of trials can be found in [Characteristics of included studies](#) and [Characteristics of excluded studies](#).

Results of the search

The electronic searches of databases and trial registers retrieved 91 and 10 records, respectively, for a total of 101 records after removal of duplicates. Our search of the FDA website identified no reports of studies. We excluded 88 records based on titles and abstracts. We examined the full texts of the remaining 13 records. We included one report corresponding to one trial (Grimminger 1993). We used only published data for this trial. We excluded 12 trials. We identified no ongoing studies or studies awaiting classification.

For a further description of our screening process, see the study flow diagram (Figure 3).

Figure 3. Study flow diagram.



Included studies

Trial design

One trial was designed as a two-arm, parallel, double-blind RCT (Grimminger 1993). This trial was monocentric and located in Germany, and reported as funded by Deutsche Forschungsgemeinschaft (German Research Foundation). One of the authors was an employee of the pharmaceutical company (Fresenius AG, Oberursel) producing the assessed treatment.

Participants

The majority of the included participants were male (18/21, 86%); mean age was 39.7 years (range 21 to 65). All included participants had acute guttate psoriasis. No information on diagnosis criteria was reported. Mean total body surface involvement was $25.7\% \pm 20.4\%$, range 10 to 90 (moderate to severe psoriasis). The duration of psoriasis before inclusion was not reported.

Interventions

The trial compared fish oil-derived (n-3) fatty acid-based lipid emulsion (Omegaven, Fresenius, Oberursel, Germany) to soya oil-

derived (n-6) fatty acid-based lipid emulsion (Lipoven, Fresenius). For each group, 50 mL emulsion (1.05 g eicosapentaenoic and 10.5 g docosahexaenoic acid) was administered twice daily via peripheral intravenous route for 10 days.

Outcomes measured

The study measured the improvement of guttate psoriasis with three distinct clinical variables: erythema, infiltration, desquamation, each on a scale of 0 to 4 on 11 areas (head, breast, back, abdomen, anogenital area, upper arms, forearms, hands, upper and lower thighs, and feet). The scores on each surface were summed (score: 0 to 44 for each variable). The clinical score was assessed every day from day 1 to day 10.

The authors also measured the change in overall subjective score (5 to 50), which was self assessed daily (from day 1 to day 10) by participants. This score was based on five items (appearance of lesions, impairment of daily life, pruritus, burning, and pain), each on a scale from 1 (worst) to 10 (best). This score was not validated.

Excluded studies

We excluded a total of 12 studies from the review based on full text ([Characteristics of excluded studies](#)). Three of these were excluded because the published data did not report separate results for participants with guttate psoriasis, and despite our efforts to contact the authors we were unable to obtain this information. We excluded three studies that evaluated other conditions (chronic plaque psoriasis); one study because the intervention assessed was an antistreptococcal treatment; and five studies that were not RCTs.

Studies awaiting classification

We did not find any studies awaiting classification.

Ongoing studies

We did not find any ongoing studies.

Risk of bias in included studies

We assessed risk of bias for the unique included trial ([Figure 4](#); [Figure 5](#)) ([Grimminger 1993](#)).

Figure 4. Risk of bias graph: review authors' judgments about each risk of bias item presented as percentages across all included studies.

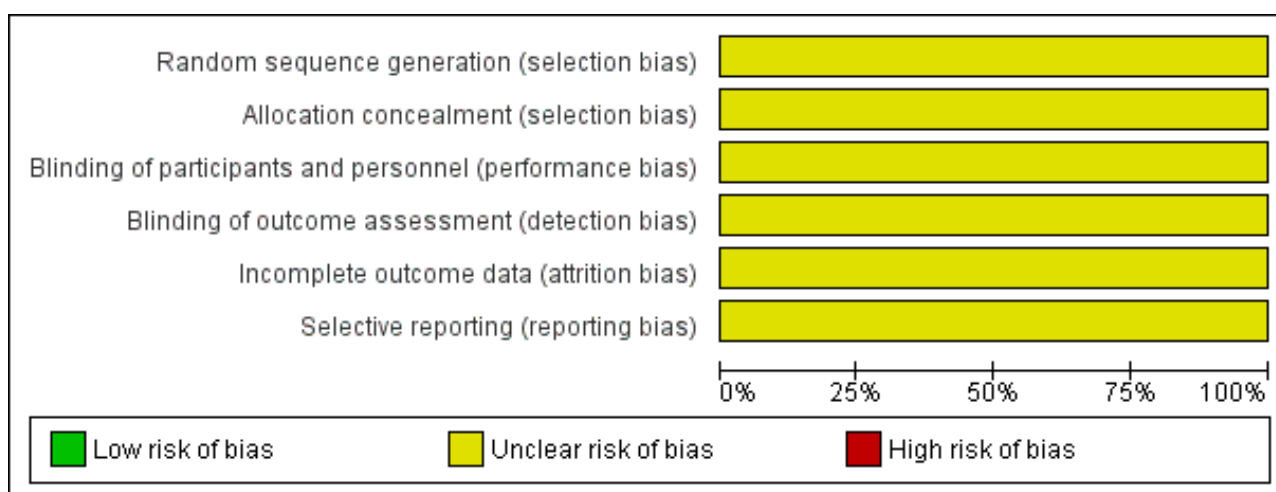
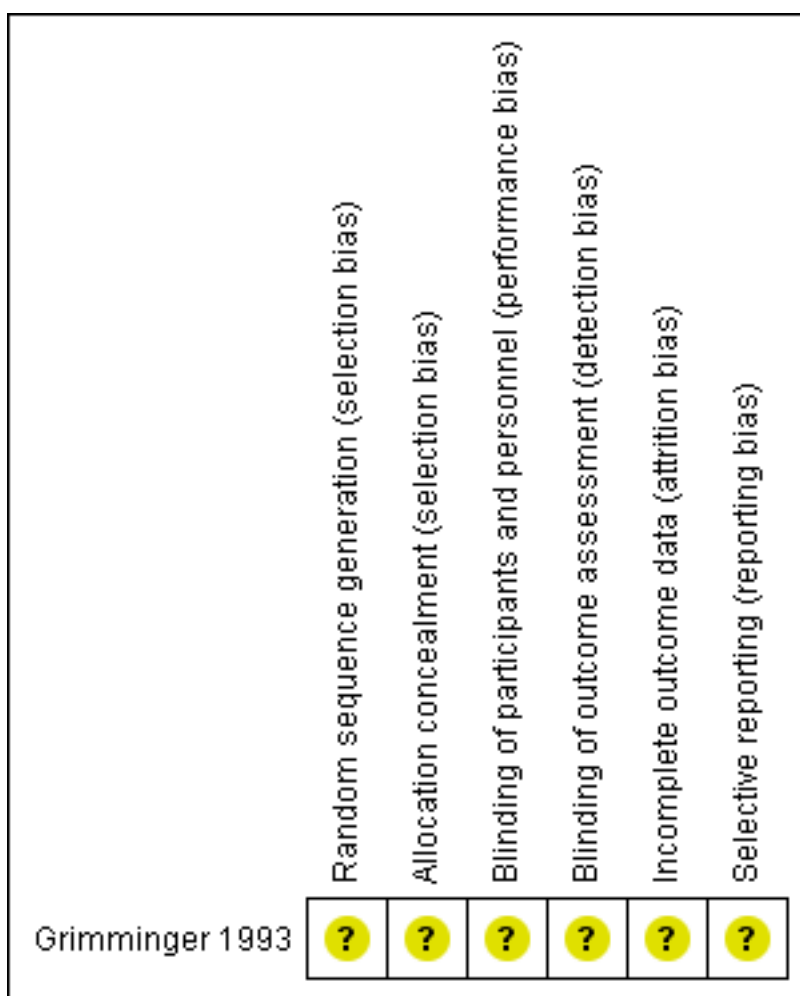


Figure 5. Risk of bias summary: review authors' judgments about each risk of bias item for each included study.



Allocation

Random sequence generation and the process to guarantee allocation concealment were not reported, therefore we considered the risk of bias as unclear.

Blinding

The included trial was reported as double-blinded, with no information provided on the specific measures taken to guarantee the blinding. As the treatment in both groups was intravenous with an emulsion, we considered the risk of bias as unclear for blinding of participants and outcome assessors, as there was no precise information on measures used to guarantee allocation concealment and assessor blinding.

Incomplete outcome data

The number of analysed participants was not reported. One participant withdrew out of 10 in the n-3 group and none in the n-6 group. To note, one participant dropped out of the n-3 group on the first day of the study but was substituted according to the random list. The method for dealing with missing data was not specified, and the reasons for withdrawal were not reported. We therefore considered the risk of bias as unclear.

Selective reporting

No registration form was available for this trial, which was published in 1993; we did not find prespecified primary or secondary outcomes. We rated the trial as at unclear risk of reporting bias.

Effects of interventions

See: [Summary of findings for the main comparison](#) Intravenous soya oil-derived (n-6) fatty acid-based lipid emulsion compared to intravenous fish oil-derived (n-3) fatty acid-based lipid emulsion for guttate psoriasis

Intravenous fish oil-derived (n-3) fatty acid-based lipid emulsion compared to soya oil-derived (n-6) fatty acid-based lipid emulsion

One trial assessed this comparison (10 participants in the fish oil-derived (n-3) fatty acid-based lipid emulsion, and 11 participants in the soya oil-derived (n-6) fatty acid-based lipid emulsion group) ([Summary of findings for the main comparison](#)) (Grimminger 1993).

Primary outcomes

Percentage of participants clear or almost clear, that is obtaining PASI 100/90 and/or PGA of 0 or 1 in the short term (up to 8 weeks of treatment)

The included trial did not measure this outcome. The maximum evaluation day was day 10.

Percentage of participants with adverse effects and severe adverse effects

The included trial did not measure this outcome. The study authors reported that adverse effects of the lipid infusion regimens were restricted to rare irritation of skin at the site of peripheral intravenous route, without providing the number of affected participants.

Secondary outcomes

Number of relapses of guttate psoriasis or flares within a period of six months after the treatment has finished

The trial did not measure this outcome. The latest clinical evaluation was performed at 10 days.

Percentage of participants achieving a PASI 75 or PGA of 1 or 2

The included trial did not measure this outcome.

Improvement in participant satisfaction measures and quality of life assessment measures

The study reported through figures the percentage of improvement of an overall subjective score (worst total score 5; best total score 50) based on five items (appearance of lesions, impairment of daily life, pruritus, burning, and pain), each on a scale from 1 (worst) to 10 (best). Results were extracted at 10 days using a web tool ([WebPlotDigitizer](#)). The score improved from 19.1 on day zero to 33.4 on day 10 (change = 14.3 points, or 75% improvement between baseline and 10 days) in the fish oil-derived (n-3) fatty acid-based lipid emulsion group, and from 25.4 on day zero to 30 on day 10 (change = 4.6 points, or 18% improvement between baseline and 10 days) in the soya oil-derived (n-6) fatty acid-based lipid emulsion group. The trial report did not provide the associated standard deviations or confidence intervals. The number of analysed participants was not available.

DISCUSSION

Summary of main results

This review included one trial comparing fish oil-derived (n-3) fatty acid-based lipid emulsion to soya oil-derived (n-6) fatty acid-based lipid emulsion administered intravenously twice daily for 10 days in 21 hospitalised adult participants ([Summary of findings for the main comparison](#)) ([Grimminger 1993](#)).

The study did not measure either the primary outcomes of the review (percentage of participants clear or almost clear, i.e. obtaining PASI 100/90 and/or PGA of 0 or 1 in the short term; and percentage of participants with adverse effects and severe adverse effects) or two of the three secondary outcomes (number of relapses of guttate psoriasis or flares within a period of six months after the treatment has finished; and percentage of participants achieving a PASI 75 or PGA of 1 or 2). However, the study authors did report that there was rare skin irritation at the site of injection, but the number of affected participants was not provided.

The study did measure improvements between baseline and day 10, as assessed by participants themselves daily using a non-validated score; this involved appearance of lesions, impairment of daily life, pruritus, burning, and pain. Improvements were greater in the fish oil-derived (n-3) fatty acid-based lipid emulsion group compared with the soya oil-derived (n-6) fatty acid-based lipid emulsion group (75% versus 18%, respectively). However, this result was based on very low-quality evidence, meaning we are uncertain of its validity.

Risks related to intravenous infusion during 10 days can be suspected but were not described in the study report.

Overall completeness and applicability of evidence

The identified study was not sufficient to address all of the objectives of the review. We found no evidence for systemic (e.g. acitretin, methotrexate), biologic (e.g. infliximab, etanercept), or topical treatment (e.g. topical corticosteroids) used in guttate psoriasis. (We did not consider antistreptococcal interventions, as these are assessed in another ongoing Cochrane Review.) We found three trials assessing phototherapy or phototherapy associated with etretinate. However, we excluded these studies as separate results for participants with guttate psoriasis were not available for these trials, which included participants with different types of cutaneous psoriasis. We found no trials assessing interventions for guttate psoriasis in children, even though this form of psoriasis is known to occur more frequently in the young. We found no trials assessing interventions for flare of guttate psoriasis in people with chronic plaque psoriasis.

The only included trial was a small exploratory trial assessing a non-conventional treatment of intravenous fish oil-derived (n-3) fatty acid-based lipid emulsion. Furthermore, this trial included only adults, while guttate psoriasis is known to occur more frequently in children.

The included study did not report our safety outcome (except for the authors stating that there was some skin irritation at the injection site), nor did it report relapse or flares within six months of treatment stopping; clearance assessed by obtaining PASI 100/90 and/or PGA of 0 or 1 in the short term; or percentage of participants achieving PASI 75 or PGA of 1 or 2. The one reported outcome was a participant-assessed improvement score based on the subjective assessment of five items. This was measured daily from baseline to day 10. The trial reported no long-term evaluation of efficacy or tolerance outcomes.

No additional trial assessing this treatment in psoriasis, and specifically in guttate psoriasis, has been carried out since 1993. Moreover, 10 days of hospitalisation is a very long duration for a disease that does not usually require hospitalisation.

Quality of the evidence

The only included trial assessed intravenous soya oil-derived (n-6) fatty acid-based lipid emulsion compared to intravenous fish oil-derived (n-3) fatty acid-based lipid emulsion, and measured only one of our outcomes (improvement in participant satisfaction measures and quality of life assessment measures). The quality of evidence was very low for this one result. We downgraded the quality of the evidence one level for serious indirectness because the trial included only adults and was provided during hospitalisations; one level for serious risk of bias as all domains

were unclear (due to poor reporting of methods in the publication); and one level due to serious imprecision, as the trial included only 21 participants ([Summary of findings for the main comparison](#)).

Potential biases in the review process

Despite our thorough search in various databases, it is possible that we overlooked trials, especially with regard to studies focusing on plaque psoriasis that might also have included participants with guttate psoriasis. However, in the previous version of this Cochrane Review ([Chalmers 2001](#)), the review authors additionally investigated 100 psoriasis trials and 112 trials on phototherapy for psoriasis, and did not identify among them stratified data for guttate psoriasis. Despite our attempt to obtain separate results for guttate psoriasis in three trials assessing phototherapy in participants with different forms of cutaneous psoriasis by contacting the authors of these trials ([Table 1](#)), our inclusion of only one trial prevented us from performing quantitative analyses.

Agreements and disagreements with other studies or reviews

The previous Cochrane Review of randomised trials in people with guttate psoriasis, [Chalmers 2001](#), only included the one same trial ([Grimminger 1993](#)).

The Cochrane Review assessing the effects of narrow-band ultraviolet B (NB-UVB) phototherapy versus broad-band ultraviolet B or psoralen ultraviolet A (PUVA) photochemotherapy for psoriasis, [Chen 2013](#), concluded that NB-UVB plus retinoid and PUVA plus retinoid are similarly effective in treating people with chronic plaque psoriasis or guttate psoriasis based on one study ([Green 1992](#)). We did not include this study because despite our request to the authors we were unable to obtain separate results for participants with guttate psoriasis.

AUTHORS' CONCLUSIONS

Implications for practice

There is no evidence to date regarding conventional topical and systemic drugs, biological therapy, or phototherapy for acute guttate psoriasis or an acute guttate flare of chronic psoriasis.

(We did not consider drugs that aimed to eradicate streptococcal infection because these are assessed in another Cochrane Review.)

We included one trial comparing fish oil-derived (n-3) fatty acid-based lipid emulsion to soya oil-derived (n-6) fatty acid-based lipid emulsion; however, the results of the study are uncertain due to very low-quality evidence.

Implications for research

This review highlights the need for trials assessing phototherapy and topical and systemic drugs for guttate psoriasis.

Population: There is a need for randomised controlled trials that assess interventions in specific populations (children/young adults with acute guttate psoriasis, and adults with a guttate flare of chronic plaque psoriasis).

Intervention: Phototherapy, topical treatment, and systemic treatment.

Comparator: As guttate psoriasis usually resolves spontaneously in a few weeks, and no treatment has demonstrated its efficacy for this form of psoriasis, a placebo control group would be adequate.

Outcomes: Outcomes should include quality of life measures, short-term clinical clearance, and long-term assessment to determine if treatment of a first acute flare of guttate psoriasis impacts long-term evolution into chronic plaque psoriasis. Future trials should also fully report harms. Trialists should contact the Cochrane Skin Group Outcome Set Initiative (CSG-COUSIN, [Schmitt 2016](#)) regarding psoriasis outcome assessments in randomised controlled trials. Adherence to guidelines such as the CONSORT statement would help in ensuring complete reporting ([Schulz 2010](#)).

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CHARACTERISTICS OF STUDIES

Characteristics of included studies [ordered by study ID]

Grimminger 1993

Methods	Study design: double-blind, randomised, 2-arm parallel trial Setting: single centre, Giessen, Germany Period: October 1990 to November 1991
Participants	Inclusion criteria: not reported Exclusion criteria: people receiving systemic psoriasis treatment (methotrexate, etretinate, PUVA, corticosteroids); people with accompanying diseases or therapeutic regimens unrelated to psoriasis; external corticosteroid application was stopped at least 5 days before entering the study Participants: 21 adults with guttate psoriasis (10/11)

Grimminger 1993 (Continued)

Baseline characteristics: acute guttate psoriasis, 18 males (86%); mean age: 39.7 years (range 21 to 65); mean BSA: 25.7% \pm 20.4%

Interventions	<p>Intervention 1: fish oil-derived (n-3) fatty acid-based lipid emulsion (Omegavenös, Fresenius, Oberursel, Germany), administered intravenously (infusion time: 1 hour), 50 mL per infusion (1.05 g eicosapentaenoic and 10.5 g docosahexaenoic acid), twice daily, during 10 days</p> <p>Intervention 2 (comparator): soya oil-derived (n-6) fatty acid-based lipid emulsion (Lipovenös, Fresenius, Oberursel, Germany), administered intravenously (infusion time: 1 hour), 50 mL per infusion (1.05 g eicosapentaenoic and 10.5 g docosahexaenoic acid), twice daily, during 10 days</p> <p>Only accepted additional psoriasis therapy: topical application of 0.03% cignolin Vaseline</p>
Outcomes	<p>Outcomes (no precision on primary or secondary outcomes):</p> <ul style="list-style-type: none"> Improvement of clinical score, assessed daily by 2 physicians working independently (the clinical score system includes 3 variables assessed separately (erythema, infiltration, desquamation), each assessed on a 0-to-4 scale on 11 areas: head, breast, back, abdomen, anogenital region, upper arms, forearms, hands, upper and lower thighs, and feet; the scores on each surface were summed (score: 0 to 44 for each variable)). The clinical score was assessed every day from day 1 to day 10. Change in overall subjective score (5 to 50), which was self assessed daily (from day 1 to day 10) by participants. This score was based on 5 items (appearance of lesions, impairment of daily life, pruritus, burn, and pain), each on a scale from 1 (worst) to 10 (best). Change in blood levels of lipid mediators at days 1, 3, 5, 10, and 40
Notes	Study funded by Deutsche Forschungsgemeinschaft and Fresenius AG, Oberursel.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	<p>QUOTE: "A double-blind randomised 10-day trial"; "random"</p> <p>COMMENT: no description on random sequence generation</p>
Allocation concealment (selection bias)	Unclear risk	COMMENT: no information was given on measure to guarantee allocation concealment
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	<p>QUOTE: "A double-blind randomised 10-day trial"</p> <p>COMMENT: no information on methods used to guarantee blinding of participants and personnel</p>
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	<p>QUOTE: "A double-blind randomised 10-day trial"; "During the trial, daily morning scoring was performed"</p> <p>COMMENT: no explanation on who assessed and the process to guarantee blinding of assessor</p>
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	<p>QUOTE: "One patient dropped out of the n-3 group on the first day of the study and was substituted according to the random list"</p> <p>COMMENT: number of randomised participants: 10/11. Number of analysed participants: not reported. Number of withdrawals: 1 out of 10 in the n-3 group and none in n-6 group.</p> <p>The method for dealing with these missing data was not specified; another participant from the n-3 group dropped out at day 1 (reason not provided) and was replaced.</p>

Grimminger 1993 (Continued)

Selective reporting (re-
porting bias)

Unclear risk

COMMENT: we did not find any prespecified primary or secondary outcomes and so could not assess reporting bias.

BSA: body surface area

PUVA: psoralen and ultraviolet A

Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
Bittiner 1988	Other condition (chronic plaque psoriasis)
Boztepe 2006	No separate data available for participants with guttate psoriasis
Caca-Biljanovska 2002	Antistreptococcal for 1 study and another condition for the other study (generalised psoriasis)
Gokdemir 2005	Observational study
Gomez 1996	Observational study
Green 1992	No separate data available for participants with guttate psoriasis
Gupta 1989	Other condition (chronic plaque psoriasis)
Hofmann 1980	Non-randomised study
Leviav 2004	Only 1 case of guttate psoriasis among participants
Melski 1977	No separate data available for participants with guttate psoriasis
O'Daly 2009	Observational study
Tas 2004	Observational study

ADDITIONAL TABLES
Table 1. Details of contacting authors

Study/author contacted	Contact	Date	Reply
Melski 1977	Retired, no contact details found		
Boztepe 2006 Prof Gonca Elçin	Characteristics and results for participants with guttate psoriasis	9 August 2017; 28 August 2017	No response
Green 1992	Characteristics and results for participants with guttate psoriasis	14 August 2017	Data no longer available

Table 1. Details of contacting authors (Continued)

Prof Cathy Green			
Grimminger 1993	<ul style="list-style-type: none"> How random sequence generation was obtained How allocation to one of the two treatments was managed to guarantee allocation concealment 	6 September 2017	No response
Prof Friedrich Grimminger	<ul style="list-style-type: none"> Diagnosis criteria for guttate psoriasis: clinical: histological Mean duration of guttate psoriasis before inclusion: treatment group: control group Number of participants clear or almost clear in the short term (up to eight weeks of treatment group: control group) Number of participants with adverse effects and severe adverse effects: treatment group: control group Baseline score for patient outcome reporting (subjective score) were treatment for treatment group 19.1 ± 2.5 and for control group 25.4 ± 2.8 what were mean score +/- SD at 10 days? 		

SD: standard deviation

APPENDICES

Appendix 1. Cochrane Skin Group Specialised Register/CRS search strategy

(guttat* or eruptive) and psoria*

Appendix 2. CENTRAL (Cochrane Library) search strategy

#1 MeSH descriptor: [Psoriasis] this term only
#2 psoria*.ti,ab,kw
#3 #1 or #2
#4 (guttat* or eruptive):ti,ab,kw
#5 #3 and #4

Appendix 3. MEDLINE (Ovid) search strategy

1. Psoriasis/
2. psoria\$.ti,ab.
3. 1 or 2
4. (guttat\$ or eruptive).ti,ab.
5. 3 and 4
6. randomized controlled trial.pt.
7. controlled clinical trial.pt.
8. randomized.ab.
9. placebo.ab.
10. clinical trials as topic.sh.
11. randomly.ab.
12. trial.ti.
13. 6 or 7 or 8 or 9 or 10 or 11 or 12
14. exp animals/ not humans.sh.
15. 13 not 14
16. 5 and 15

[Lines 6-15: Cochrane Highly Sensitive Search Strategy for identifying randomized trials in MEDLINE: sensitivity- and precision-maximizing version (2008 revision)]

Appendix 4. Embase (Ovid) search strategy

1. exp guttate psoriasis/
2. psoria\$.ti,ab.

3. exp psoriasis/
4. 2 or 3
5. (guttat\$ or eruptive).ti,ab.
6. 4 and 5
7. 1 or 6
8. crossover procedure.sh.
9. double-blind procedure.sh.
10. single-blind procedure.sh.
11. (crossover\$ or cross over\$).tw.
12. placebo\$.tw.
13. (doubl\$ adj blind\$).tw.
14. allocat\$.tw.
15. trial.ti.
16. randomized controlled trial.sh.
17. random\$.tw.
18. or/8-17
19. exp animal/ or exp invertebrate/ or animal experiment/ or animal model/ or animal tissue/ or animal cell/ or nonhuman/
20. human/ or normal human/
21. 19 and 20
22. 19 not 21
23. 18 not 22
24. 7 and 23

Appendix 5. LILACS search strategy

((guttat\$ or gutata or gotas) and (psoria\$))

In LILACS we searched using the Controlled clinical trials topic-specific query filter and the above terms.

CONTRIBUTIONS OF AUTHORS

AM was the contact person with the editorial base.

AM co-ordinated contributions from the co-authors and wrote the final draft of the review.

AM and NS screened papers against eligibility criteria.

AM obtained data on ongoing and unpublished studies.

AM, RAH, MS, ET, NS, LLC appraised the quality of papers.

MS and RAH, LLC extracted data for the review and sought additional information about papers.

AM and MS, LLC entered data into Review Manager 5.

AM, MS, RAH, NS, ET, LLC analysed and interpreted data.

ET, LLC, AM, MS worked on the methods sections.

AM, MS, ET drafted the clinical sections of the Background and responded to the clinical comments of the referees.

ET responded to the methodology and statistics comments of the referees.

CH was the consumer co-author and checked the review for readability and clarity, as well as ensuring outcomes are relevant to consumers.

LLC is the guarantor of the update.

Disclaimer

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DECLARATIONS OF INTEREST

Annabel Maruani: Nothing to declare.

Mahtab Samimi: received fees for speaking at educational programs (BMS) and travel, accommodation and meeting expenses (Novartis, Galderma International, Janssen-Cilag, Cosmetique Active France, NAOS, MSD-France, Shire) that are unrelated to this review.

Natasha Stembridge: Nothing to declare.

Rania Abdel Hay: Nothing to declare.

Elsa Tavernier: Nothing to declare.

Carolyn Hughes: Nothing to declare.

Laurence Le Cleach: Nothing to declare.

Key Editor, Gloria Sanclemente: I do not have current or past affiliations or other involvement in any organisation or entity with an interest in the outcome of this review. I have not been involved in any study included in this review, but in the last three years, I have received

sponsoring for attending scientific meetings or congresses by Janssen-Cilag, Novartis, and AbbVie. I also declare that I am currently co-ordinating a Diploma in Evidence-Based Dermatology in which attendees have been sponsored by Pfizer, AbbVie, and Novartis laboratories.

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Internal sources

- No sources of support supplied

External sources

- The National Institute for Health Research (NIHR), UK.

The NIHR, UK, is the largest single funder of the Cochrane Skin Group.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

Title, Abstract, Plain language summary, and Objectives: We changed "Interventions for guttate psoriasis" to "Non-antistreptococcal interventions for acute guttate psoriasis or an acute guttate flare of chronic psoriasis" to better indicate the scope of the review.

Methods > Criteria for considering studies for this review > Types of participants: We added the following sentence, which was initially omitted in the protocol: "We excluded trials that did not have separate data for guttate psoriasis patients (not available in published or unpublished data or through requests to the author)."

Methods > Data collection and analysis > Selection of studies: We deleted the end of the sentence: "We contacted study authors for clarification when necessary *in case trials were published in the previous 10 years, i.e. 2006.*"

Methods > Data collection and analysis > Assessment of risk of bias in included studies: We clarified that we did not assess the domain 'other bias' because there were no methodological concerns in addition to the other domains assessed.

Methods > Data collection and analysis > Dealing with missing data: We expanded this section to describe how we would handle missing outcome data. We planned to use simple imputation methods and to assume that all missing data were either events or non-events ([Higgins 2011b](#)). However, the data reported in the only included study did not permit use of this method.

INDEX TERMS

Medical Subject Headings (MeSH)

Administration, Oral; Administration, Topical; Biological Therapy; Immunosuppressive Agents [therapeutic use]; Phototherapy; Psoriasis [*therapy]; Treatment Outcome

MeSH check words

Humans